A Framework and Case Study for VCCEP Exposure Assessment

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EXECUTIVE SUMMARY

The purpose of this document is to propose an example of a framework for developing an exposure assessment for the Voluntary Children's Chemical Evaluation Program (VCCEP), and to illustrate this framework with a case study. The VCCEP is an EPA-sponsored voluntary pilot program "designed to provide data to enable the public to better understand the potential health risks to children" (Federal Register, December 26, 2000). Chemical companies have volunteered to sponsor assessments for 20 chemicals for this pilot. The VCCEP is designed as a three-tier process, with each successive tier requiring more hazard data and a more refined exposure assessment. The first tier of exposure assessment is based on readily available information and does not require the generation of new data. The framework and case study presented in this document largely focuses on the first tier of the VCCEP. While the case study developed to illustrate the proposed framework used a fictional chemical with a robust set of hazard data and a simplified set of potential exposure pathways, the framework is intended to be useful for assessing chemicals with varying amounts of existing data. Further, while the case study presented here focuses on consumer applications of the subject chemical, the framework itself should be useful in identifying pathways and exposure scenarios for chemicals in a wide range of situations. The framework and case study are specific to the VCCEP, and are not meant to provide general guidance on exposure assessment for other Federal or international exposure assessment efforts.

The framework and the case study should not be viewed as a rigid format for Tier I evaluations within the EPA's VCCEP. There is no single method that is universally accepted as applicable to developing exposure assessments. While each assessment conducted for the VCCEP will be unique, the principles underlying the exposure assessments will be similar. It is expected that the actual Tier I VCCEP submissions will vary from chemical to chemical and each will be specifically focused to address the existing readily available data and chemical-specific use and exposure factors. Thus, some of the components discussed in the case study may or may not be relevant for a specific chemical. Scientific quality, completeness and transparency are key features of any exposure assessment. The intent of the VCCEP is for sponsors to develop high quality assessments that are as complete as necessary for the appropriate tier. In doing so, the calculations, model runs and derived estimates would be presented in such a way that there is sufficient detail to permit an independent evaluation of the assessment. The overall goal of the assessment is to support a scientifically sound and satisfactory risk-based characterization for a given chemical for a given tier.

The proposed framework includes three parts: (1) selection of exposure scenarios, (2) exposure and risk assessment, and (3) data needs assessment. The first part focuses on collecting the available information on the chemical (e.g., usage data, physicochemical data, environmental fate properties, hazard data, available exposure data, etc.) to

developing a list of scenarios that need to be considered in the exposure assessment. This part has seven steps:

1) Assembly of relevant information for the exposure assessment
2) Organization of sources into data bins
3) Determination of plausible exposure pathways
4) Inclusion of pathways with significant exposure to children
5) Consideration of potential receptors
6) Consideration of exposure durations
7) Development of exposure scenarios

At the end of this process, a list of scenarios is made for quantitative exposure assessment.

The second part focuses on the process of developing an exposure assessment for the scenarios. While the focus of this document is on exposure assessment, risk assessment is also discussed in the framework and case study, to allow an illustration of the tiered evaluation process in which hazard data is evaluated in the context of the exposure assessment. This serves to illustrate how a risk-based evaluative approach can be useful in refining a Tier I screening level assessment if concerns are found. The refinements illustrated in the case study may go beyond the level of detail that some VCCEP sponsors intend to include in their Tier I submissions. This part also includes an aggregate assessment to allow an assessment of the combined exposure from different pathways. The third part of the framework is the data needs assessment. This part relates to the assessment of data needs for the next tier of the VCCEP, if concerns were found in the previous tier. This is recognized as a part of the VCCEP, but is not included in the case study, which focuses on a Tier I assessment.

For the case study, a hypothetical chemical called Seussium grinchate (SGA) was developed to illustrate the framework. Although this is a hypothetical substance, realistic physical, chemical, and toxicological properties were assigned to make this case study applicable and relevant. The hypothetical substance SGA is described as a solvent used in the manufacture of carpets, a component of various household cleaners, and in food extraction. It is also designated as a chemical intermediate for several chemical processes. When used as a chemical intermediate, it is fully consumed. Thus, there are no exposure concerns for SGA's use as a chemical intermediate. From a hazard standpoint, it was assigned low acute toxicity, but is described as toxic by ingestion and inhalation for chronic exposures, and designated as a developmental toxicant and a carcinogen by the inhalation route.

In this case study, the framework was used to develop a set of exposure scenarios for quantitative analysis, focusing the Tier I assessment on those exposure scenarios of greatest concern for evaluating children's exposures and potential health risks. The case

study example also indicates operation of the framework to identify exposure scenarios that are of negligible concern for the risk assessment.

Quantitative exposure estimates were generated for each of the exposure scenarios of concern. For several scenarios, including inhalation, ingestion of food, and dermal contact with carpet, the screening level Tier I evaluation process (in which hazard data is considered in the context of the exposure assessment) showed possible concerns for the screening-level assessment. For each of these pathways, the case study includes a refined assessment, using either more sophisticated estimation techniques or collection of new data (the Tier I exposure assessment under the VCCEP does not require collection of new data); the refined assessment showed no concerns. An aggregate assessment was also conducted, which showed no concerns.

I. INTRODUCTION

The purpose of this document is to propose an example of a framework for developing an exposure assessment for the Voluntary Children's Chemical Evaluation Program (VCCEP), and to illustrate this framework with a case study. Both the structure and the content of the framework are designed to meet the specific policy and technical objectives of the U.S. EPA's VCCEP, and reflect both policy and practical judgement. Therefore, neither the framework nor this document should be used as a template or guidance for exposure assessment in other domestic or international contexts. This document focuses on Tier I of the exposure component of the VCCEP program, and includes suggestions for the following activities:

- Gathering the necessary information for a children's exposure assessment.
- Categorizing sources of exposure into manageable data bins that feed information into the exposure assessment for potential pathways.
- Selecting plausible exposure pathways from the universe of possible pathways, including the elimination from consideration of pathways that are not of concern, and the basis for their elimination.
- Estimating exposures for the plausible pathways, at a screening level.
- Establishing relevant receptor populations and associated activity patterns.
- Refining the exposure assessment with known information before proceeding to the collection of new data (in Tier I if a sponsor wishes to or at a higher tier).
- Integrating estimated exposures with relevant hazard data to characterize risks associated with the estimated exposures. While this document focuses on the exposure assessment aspect of the VCCEP, the case study includes a risk assessment to allow a demonstration of the tiered process of exposure assessment (i.e., refinements made after concerns are found in screening level analyses)
- Characterizing uncertainties associated with the exposure assessment.

A hypothetical chemical has been developed for the case study. The hypothetical chemical is called Seussium grinchate (SGA) (A Dr. Seuss theme is used throughout the assessment; e.g., the largest plant for SGA production is in Whoville). SGA was designated a solvent used in the manufacture of carpets, a component of various household cleaners, and a solvent used in food extraction.

The VCCEP is an EPA-sponsored voluntary pilot program "designed to provide data to enable the public to better understand the potential health risks to children" (Federal Register, December 26, 2000). Chemical companies have volunteered to sponsor assessments for 20 chemicals for this pilot. The VCCEP is designed as a tiered process, with each successive tier requiring more hazard data and a more

refined exposure assessment. For Tier I, the human health studies from the HPV Challenge Program are required. However, when conducting a Tier I assessment, all readily available toxicological data should be considered in the risk assessment. For chemicals proceeding to Tier II, additional testing may be required including genetic toxicity testing, 90-day subchronic toxicity, 2-generation reproductive toxicity, prenatal developmental toxicity in two species, immunotoxicity, and uptake and metabolism studies. For chemicals proceeding to Tier III, additional testing for chronic toxicity and/or carcinogenicity, adult neurotoxicity, and developmental neurotoxicity may be required.

For each of the three tiers, the VCCEP requires four types of assessments: (1) a hazard assessment, (2) an exposure assessment, (3) a risk assessment, and (4) a data needs assessment (i.e., what, if any, additional data are needed in the next tier). The foundation of the VCCEP pilot program is its risk-based approach. The VCCEP pilot is structured upon a tiered evaluation process in which hazard data are evaluated in the context of exposure assessment. Because this document focuses on exposure, only a brief review of hazard data is provided, but a more detailed exposure assessment is developed. For the purposes of this document, the exposure and risk assessment are included in one section as an example of a method of integrating the hazard and exposure assessments for each pathway to better understand the tiered risk-based approach.

Although this case study illustrates an example of possible exposure-related submissions for the VCCEP program, sponsors may choose the level of detail for their own submissions based on scientific and professional judgement. This document presents examples of both screening level assessments using conservative defaults, and more refined assessments. The framework that is presented is designed to be flexible in regard to the levels of detail and refinement that are necessary. The goal of the case study is simply to demonstrate the practicality of the proposed framework by presenting potential areas to consider in a robust exposure assessment.

The remainder of this document is organized as follows:

- *Section II*: Proposed Framework for Developing a Tier I Exposure Assessment
- *Section III*: Hazard Assessment for the Case Study (Only a brief review of hazard data for the case study is provided, as this report focuses on exposure. The brief review provides a listing of relevant toxicological endpoints and benchmarks, as these are needed to conduct the risk assessment).
- *Section IV*: Exposure Assessment for Case Study

It is recognized that a data needs assessment is also a component of the VCCEP, but it is not included in this case study, as the focus is on a Tier I exposure assessment.

II. PROPOSED FRAMEWORK FOR DEVELOPING A TIER I EXPOSURE ASSESSMENT

This chapter presents a proposed framework for developing a Tier I exposure assessment. This framework has been designed to be consistent with EPA Guidelines for Exposure Assessment (EPA, 1992). The framework is based on a scientifically sound paradigm for evaluating children's exposures in a way that parallels the level of detail in the safety testing. The framework provides the requisite scientific rigor for designing and conducing a Tier I exposure assessment while maintaining sufficient flexibility to support information needs for various levels of detail that may be needed for the diverse chemical and uses expected under the VCCEP.

Conceptually, the exposure assessment process under the VCCEP has three basic elements:

1) Understand how a specific chemical flows through commerce sufficiently to identify where exposures to children could occur.
2) Determine the plausible pathways by which a chemical might reach children, and assess, at least qualitatively, whether these may result in potentially meaningful and relevant exposures to children.
3) Estimate exposures for potentially meaningful and relevant situations, using available screening level approaches, such as predictive models and/or direct observations. This evaluation may also include assessing the potential for aggregate exposure (where an individual child may be exposed simultaneously to the same chemical through several pathways.)

The purpose of this framework is to both describe the process and provide guidance on developing a Tier I exposure assessment for the VCCEP pilot. The framework provides the means to:

- Aggregate multiple sources of exposure into data bins that represent a common exposure pathway. The data bins help feed related pieces of exposure information into the exposure assessment by potential pathways.

- Develop a list of plausible exposure pathways for a chemical. A pathway is defined as exposure in a separate microenvironment by a particular route (e.g., ingestion, dermal, or inhalation). For example, inhalation exposure to indoor air is considered a pathway. The framework also provides guidance on how to narrow the list of plausible exposure pathways to a priority set of pathways of potential concern that warrants a quantitative estimate of exposure.

- Identify receptor populations and associated activity patterns.

- Include or eliminate available information on appropriate durations, frequencies, or timing of exposures based on significant toxicological endpoints or receptor data (e.g., subpopulations).

- Illustrate the tiered process of exposure and risk assessment, and to illustrate approaches whereby exposure assessments may be refined as much as possible before proceeding to new data collection. This illustrates how the assessment and refinement serves to focus on parameters and data that may reduce the uncertainty in the assessment.

The framework has three parts with multiple steps in the first and second parts as follows:

Part 1: Selection of Exposure Scenarios

1) Assembly of relevant source information for the exposure assessment. This step may include collection of readily available information. Examples of this information include production volumes and manufacturing and processing release amounts, industrial, institutional, and consumer uses of the product, outside the chain of commerce sources, disposal amounts, physicochemical properties, environmental fate properties, hazard data, and exposure data. The outside the chain of commerce sources includes natural sources, biological sources, fuels, combustion products, etc., and may be important for many VCCEP chemicals. This step may also include a description or list of usages of the chemical that may result in exposure. It is important to recognize that the amount and type of available information for different chemicals will vary.

2) Organization of sources into data bins: A data bin is an aggregation of multiple chemical sources that can contribute to the same exposure pathway. In this step, sources are aggregated for exposure by the same pathway in the same microenvironment, if possible. This step can be initiated when multiple sources are identified each of which contributes to exposure by the same pathway in a defined microenvironment. The purpose of this step is to reduce the universe of exposure sources, if possible, into more manageable groups of sources. This may be particularly important for chemicals that are used in numerous consumer products, and for which it is difficult to separately estimate exposure for each product. For example, if a chemical is used in dozens of household products and is volatile, then the indoor use of these products may result in inhalation exposure of indoor air. These products can be aggregated into one data bin for exposure assessment. From this bin, inhalation exposure to indoor air would be estimated. Sources should be

aggregated into as many data bins as is logical, to reduce the number of sources for the exposure assessment.

The aggregation of sources into these data bins determines whether to do a "top-down" or "bottom-up" approach for particular pathways. For example, a "bottom-up" approach for inhalation of indoor air might develop an estimate of the exposure contribution for a series of different products in which the chemical is used, and sum the contributions to get the total exposure concentration. This approach would make sense if the chemical is used in relatively few products, and has the advantage of attributing total exposure to individual products. However, if the chemical is used in numerous products, a "top-down" approach might be more appropriate, which may mean simply using available indoor air measurements from all sources together to estimate total exposure, without necessarily examining each source individually.

3) Determination of plausible exposure pathways: This step will include a listing of all plausible exposure pathways, including ingestion, inhalation, and dermal exposure, for children based on the available information on the chemical. Hazard data should be considered in this step as the relevant endpoints could impact the type of exposure scenarios to be considered. For example, if developmental or reproductive toxicity concerns cannot be eliminated, adult exposure pathways may need to be considered such as occupational exposure, as well as aggregate adult exposure. Also, any available monitoring data could be considered in this step for potential exposure pathways to consider.

   The Alliance for Chemical Awareness (ACA) has developed a Flowchart for Evaluation of Human Health Exposure that may be helpful for identifying all of the potential pathways of exposure for a chemical (see http://chemicalawareness.org/toolkit/eframework.html). It is important to note that the ACA addressed exposures to all ages, not specifically children.

4) Inclusion of pathways with potentially significant exposure to children: In this step, those pathways that are of potentially greatest concern to children are identified and those plausible pathways with negligible exposure to children are removed from consideration. Sources of information for eliminating exposure pathways from consideration include physicochemical data (e.g., if the chemical is non-volatile, then inhalation exposure is unlikely), usage data (e.g., if a chemical is not used in any indoor product, then, indoor sources of exposure are not considered), and activity data for children (e.g., data that suggest that children do not engage in a certain behavior that would result in exposure). Also, in this step, any pathway that can be shown to have negligible exposure though monitoring results may be eliminated.

It is important to note that ultimately aggregate exposures may need to be considered in the VCCEP. Therefore, caution is urged prior to simply eliminating a particular pathway because it appears to be below the level of concern when considered alone, because when combined with other exposures, aggregate exposure could be a concern. However, there needs to be some reasonable judgment through monitoring or other available exposure data to eliminate pathways that are clearly negligible. The criteria for eliminating an exposure pathway as negligible is that the exposure is below the level of concern and that it adds negligibly to the aggregate exposure (e.g., the exposure is at least 100-fold less than the aggregate exposure)[1].

The most likely source of data for eliminating a pathway is exposure or microenvironmental monitoring data. For example, if a particular chemical was sampled for but not detected (with an adequate detection limit) in EPA's Total Exposure Assessment Methodology (TEAM) indoor air monitoring program (a large multi-city monitoring program of indoor air concentrations and exposures), inhalation of indoor air may be eliminated from the universe of plausible pathways. As another example, if a company has monitoring data to show that there are no significant exposures downwind of their facility, then inhalation exposure to children living near the facility may be eliminated from consideration.

5) Consideration of potential receptors: Given all the plausible exposure pathways, the potential receptor populations should be identified, along with the associated activity patterns of the receptors. The purpose of this step is to appropriately focus consideration to relevant exposure groups. For example, it could be determined whether most children are exposed to a particular pathway, or only a particular subpopulation is exposed to that pathway. Choices of subpopulations to consider could be driven by hazard data.

6) Consideration of exposure durations: Within each exposure pathway, the appropriate exposure durations to consider should be identified. For example, if a chemical is acutely toxic then acute exposures may be important, or if a chemical is a carcinogen, then lifetime average exposure may be important. It may be possible to exclude particular exposure durations from consideration, or eliminate particular exposure durations based on toxicological endpoints of concern. For example, if a chemical only is associated with acute toxicity, then longer-term exposures might not need to be considered. If a chemical only is associated with chronic or carcinogenic toxicity, then shorter-term

[1] Of course, it would not be appropriate to eliminate a significant number of exposure pathways that added negligibly to the aggregate exposure if the sum of these pathways was significant relative to the aggregate exposure.

exposures might not need to be considered (unless the exposures significantly contribute to lifetime average exposure). If a chemical is an allergen or sensitizer, then the frequency and timing of exposure may be particularly relevant.

7) Development of exposure scenarios: In this step, the information and decisions made in steps 2 though 6 will be used to develop exposure scenarios. Scenarios will be developed for each plausible exposure pathway and duration. The next part focuses on estimating exposures and risks for each of the scenarios.

Part 2: Exposure and Risk Assessment

1) Screening-level exposure and risk assessment for exposure scenarios: For each of the exposure scenarios, a screening-level exposure and risk assessment may be conducted using readily available information and straightforward, conservative, and health protective default methodologies. If the exposure for a particular pathway is below the level of toxicological concern (accounting for appropriate safety factors), then that pathway may be eliminated from consideration, until the aggregate assessment.

2) Refined exposure and risk assessment for exposure scenarios: For pathways that the screening-level risk assessment could not eliminate from concern, the VCCEP includes options to conduct further toxicity testing or to conduct a more refined exposure assessment. As this case study focuses on exposure issues, examples of refined exposure assessments are included. The refined assessment may include use of more advanced, data-derived exposure assessment methodologies such as chemical-specific exposure factors, the use of probabilistic techniques, or the use of more refined exposure models, etc. The refined assessment could also include the collection of additional data, such as detailed stack release information and the location of residences surrounding a facility, to allow a refined dispersion modeling assessment. Another example might be the assessment of dermal exposure using a default absorption factor of 100 percent (screening assessment), followed by the generation of new data to determine a more realistic value for this exposure factor (refined assessment). It is possible that there could be additional refinements to the exposure assessment, if there are available avenues for improving the assessment.

3) Aggregate assessment: If all of the individual pathways are shown not to be of concern, then an aggregate assessment could be conducted combining those exposures for pathways that can contribute to aggregate exposure for a single child (i.e., occur to an individual close in time or in the same

microenvironment). At an initial (most conservative) stage of analysis, the aggregate exposure would be calculated as the ingestion exposure (assuming all ingested exposure is absorbed) plus the portion of the inhalation and dermal exposure that is absorbed (if information is available on absorption; if not, conservative default assumptions would be made). Additionally, if there are multiple inhalation exposure pathways, an aggregate assessment for these pathways could also be conducted. If the aggregate assessment indicates no potential concerns, no further action is needed. If the aggregate assessment indicates potential concerns, then refinements in the exposure assessment could be explored for all of the pathways that drive the initial estimate.

Another important consideration in an aggregate assessment is mass conservation. If conservative assumptions were made for various pathways, it is possible that the sum of the mass allocated to each exposure pathway may exceed the total mass emissions. If concerns are found in an aggregate assessment, one area of refinement might be a calculation to ensure that mass is conserved, and appropriate revisions in the individual pathway exposure estimates to ensure mass conservation.

Another important element of the risk assessment will be a characterization of uncertainties in the risk estimates. Within the VCCEP, it is envisioned that this will be completed as a part of the exposure and risk assessment. A qualitative uncertainty evaluation is included in this case study.

Part 3 - Data Needs Assessment: Within the VCCEP, for pathways that the refined exposure and risk assessment does not eliminate from concern, an assessment of data needs may be made for the next tier. It is recognized that this is a component of the VCCEP, but it is not included in this case study, as this document is focused on the Tier I exposure assessment.

Figure 1 illustrates the process of selecting exposure pathways for exposure assessment. This figure shows how various factors are weighed to select and eliminate from consideration different exposure pathways. The final set of the exposure pathways (and accompanying receptors and exposure durations) are the pathways for which quantitative exposure and risk estimates may be made.

Figure 2 illustrates the exposure and risk assessment process. If the initial, screening-level exposure assessment indicates a potential risk concern, the process cycles back to the exposure assessment for refinement, if possible. This cycle may continue until all available avenues of refining the exposure assessment are exhausted. If the risk assessment for the individual pathways shows no concerns, then an aggregate assessment could be conducted and refined, if necessary, until all avenues of

refinement are exhausted or until the aggregate assessment shows no concerns. There are two general methods to refine the aggregate assessment: (1) refinement of individual exposure pathway estimates that have a large impact, and (2) refinement of the aggregate exposure estimate by using data to account for the probability that particular children are simultaneously exposed by multiple pathways. If the risk assessment or aggregate risk assessment indicates a potential concern and no further refinements are possible or desirable with available data (either for individual pathways or for the aggregate assessment), then a data needs assessment may be conducted, to determine what additional hazard or exposure data can be collected to refine the assessment (e.g., next tier data needs).


Yes

III. HAZARD ASSESSMENT FOR CASE STUDY

The VCCEP requires a hazard assessment for each chemical. At the first tier, the hazard assessment should include a review of all readily available and relevant hazard data available for the chemical, and a recommendation of toxicity criteria values (e.g., reference dose) to use for risk assessment. It is acknowledged within this case study that the hazard assessment is not in the format suggested in the VCCEP *Federal Register* notice. It is beyond the scope of this case study to develop the hazard assessment in detail, as this case study focuses on exposure. Instead, a simple listing of the toxicological values to be used for the risk assessment is provided for the hypothetical chemical SGA:

- A reference dose of 1 mg/kg/day, based on statistically significant decrements in neuropsychologic test results from SGA-exposed workers at the Whoville plant (Whoton and Whoferling, 1988).

- A reference concentration of 1 mg/m^3, based on a moderate and reversible respiratory tract irritation from an occupational epidemiological study (Lorax Laboratories, 2000).

- A No Observed Adverse Effect Level (NOAEL) of 500 mg/kg/day for a pre-natal rat developmental study. The NOAEL is based on malformations in the pups. The NOAEL for effects on the dams was higher. With a standard 100-fold safety factor, the level of concern for developmental toxicity is 5.0 mg/kg/day (Whoman et al., 1998). A similar study in rabbits had a higher NOAEL (VanWho et al., 1999).

- In a 2-generation rat reproductive study, there were no reproductive effects. Therefore, SGA is not considered a reproductive toxicant.

- An inhalation cancer unit risk of $5x10^{-6}$ per $\mu g/m^3$ (Horton Consulting, 1991). SGA has been demonstrated to be not carcinogenic by ingestion (Whoton et al., 1995).

- Data show that the chemical has a very low acute toxicity, such that short-term occupational exposures are unlikely to be a concern (Whoville Industries, 1986).

- Data show that chemical is not an allergen, sensitizer, reproductive toxicant, or immunotoxicant (Whoton et al., 2000).

It is assumed that the toxicological database for this chemical is well developed with available studies to address all endpoints; thus, all relevant exposures can be considered in the first tier.

IV. EXPOSURE ASSESSMENT FOR CASE STUDY

A. ASSEMBLY OF INFORMATION FOR EXPOSURE ASSESSMENT

1. Manufacturing and Usage Data

SGA is a solvent used in the manufacture of carpets, a component of various household cleaners, and in food extraction. SGA is produced in five manufacturing plants nationwide. These plants and their production volumes and emissions are listed in Table 1 for 2000. The total production volume is 2,200 tons per year (tpy), with air emissions of 88.0 tpy and a water discharge (all to local rivers) of 2.2 tpy. The largest facility is in Whoville operated by Whoville Industries with a total production volume of 1,000 tpy, air emissions of 40 tpy, and water discharges of 1.0 tpy. SGA is also used in three plants that produce carpet, in six plants that produce household cleaners, in numerous food-processing facilities, and as an intermediate for chemical processes at two other facilities. Table 2 summarizes the volumes of SGA used for these various usages, along with the air and water emissions. The usages for SGA are as follows:

- Carpet production: 300 tpy or 13.6 percent of total volume
- Household cleaner production: 500 tpy or 22.7 percent of total volume
- Food extraction: 400 tpy or 18.2 percent of total volume
- Chemical intermediate: 1,000 tpy or 45.5 percent of total volume.

2. Physicochemical Properties and Environmental Fate

Table 3 summarizes the physicochemical properties of SGA, and Table 4 summarizes the environmental fate properties. From the standpoint of characterizing environmental exposure to children, one of the most important properties of SGA is that it degrades very quickly in water, with fast rates of aerobic biodegradation (2.5 day half-life).

3. Exposure and Biomonitoring Data

SGA has been part of several large exposure and biomonitoring studies conducted by government agencies, including:

- In EPA's TEAM study, SGA was detected in most of several thousand indoor air measurements. The concentrations ranged from 0.001 to 0.040 $\mu g/m^3$.

- In the Food and Drug Administration's (FDA's) Total Diet Study (TDS), SGA was detected in 63 percent of green eggs (average residue of 15 ppm), 72 percent of ham samples (average residue to 20 ppm), and 34 percent of red wine samples (average residue of 10 ppm).

- In the Centers for Disease Control and Prevention's (CDCP's) National Health and Examination Survey (NHANES), SGA was detected in 23 percent of human blood samples at trace quantities (average residue of 0.15 ppb)

These data provide evidence of potential exposures to SGA. While brief summaries are provided above, the exposure assessment submission for the VCCEP pilot would include more details on the design, measurement methods, and results for those studies. Also, the data that are used in the exposure assessment, and the submission would conform to the requirements of transparency and completeness for the VCCEP. In this case study example, the key hypothetical exposure investigations/references used in developing the exposure assessment are described in Appendices with a standard format. Some members may wish to provide modeling results in similarly formatted appendices, while others may prefer to describe modeling results in free text.

Additionally, Whoville Industries, the largest producer of SGA, has conducted a large exposure and biomonitoring study for men and women who work at their Whoville plant. The study was published in *Occupational Health Perspectives* and included both personal exposure measurements of inhaled SGA, and blood biomonitoring measurements (Whoford and DeWho, 1999).

B. DEVELOPMENT OF PLAUSIBLE EXPOSURE PATHWAYS

In this section, the framework for developing plausible exposure scenarios is followed for the case study, beginning with Step 2 (as Step 1, Assembly of Relevant Information for the Exposure Assessment, was presented in the last section).

Step 2 - Organization of Sources into Data Bins

SGA is used in several dozen different household cleaners, and in eight different brands of carpet. All of these products have the potential to contribute to indoor air levels. Market data are insufficient to establish a reasonable profile of how many of these cleaners or carpet materials that the typical person may have in their homes. However, reliable indoor air concentration data are available, which encompass releases from these sources. Therefore, for the purposes of estimating

indoor air exposure, the household cleaners and carpets are aggregated into a data bin, and considered as one source.

Step 3 – Determination of Plausible Exposure Pathways

Based on the usage profile and physicochemical properties of SGA, the following pathways are considered plausible:

1) Inhalation of residential indoor air, due to its presence in household products and carpet and its detections in the TEAM study.
2) Inhalation of ambient air due to the air emissions from manufacturing and production facilities, and it being a volatile chemical used in household products and carpet.
3) Inhalation of volatilized SGA from carpet surfaces for children breathing very close to the surface of the carpet.
4) Ingestion of food due to its detections in green eggs and ham, and in red wine in FDA's TDS study.
5) Ingestion of water by residents living near production or manufacturing facilities due to industrial discharges of the chemical into the drinking water watershed.
6) Ingestion of breast milk by infants, due to its detection in blood samples of women in the NHANES study.
7) Ingestion of SGA by mouthing of toys or other objects that have been in contact with carpet with SGA or have residues from use of household cleaners.
8) Dermal contact with carpet, due to its presence in carpet and because children, particularly infants, are known to play vigorously on carpets.
9) Dermal contact from use of household cleaners.
10) Occupational exposure to pregnant women, based on monitoring data in the Whoville facility by Whoville Industries, and because SGA is a developmental toxicant. These data are used to estimate aggregate exposure to pregnant women.

Acute exposures are not considered because SGA has a very low acute toxicity, and the consumer products containing SGA are manufactured with childproof closures.

Step 4 – Inclusion of Pathways with Potentially Significant Exposure to Children

EPA tracks concentrations of chemicals in drinking water in its National Drinking Water Contaminant Occurrence Database. In this database, SGA was never detected in over 2,000 samples, including several hundred samples in the watersheds of the production and manufacturing facilities. Most samples were

measured by HPLC, the preferred method for analyzing SGA in water, with a detection limit of 0.01 ì g/L, which is below EPA's Office of Drinking Water level of concern for SGA ingestion of 100 ì g/L. Also, Whoville Industries conducted a pilot wastewater plant removal efficiency study and found that 99 percent of SGA is removed in the primary treatment systems of wastewater treatment plants. Additionally, SGA degrades to a benign compound in water relatively fast by biodegradation. Therefore, the drinking water results are not surprising. For these reasons, ingestion of water was removed from consideration.

SGA has been detected in green eggs, ham, and wine in FDA's TDS study. However, children generally do not drink wine. Therefore, this exposure pathway is considered irrelevant for children, and is removed from consideration.

Horton Manufacturers (HM) conducted a study to measure the dermal exposure associated with the usage of household products containing SGA and the subsequent exposure to household surfaces where the product was used. This study found that exposures to children were all below detection limits. Additionally, the exposures were found to be at least 100 times lower than dermal exposures to children playing on carpet surfaces with SGA (based on detection limits from HM study). Therefore, this exposure pathway is not considered in this analysis.

Loraxium Carpet Manufactures (LCM) conducted a study to measure residues of SGA on carpet, the concentration of SGA in the air directly above the carpet (potentially in the breathing zone of a child playing on the carpet), and the residue on toys and other objects that children may mouth and that come in contact with SGA from carpet or household cleaners. The study showed that there are measurable residues of SGA on carpet surfaces that children may be exposed to while playing. However, the study also found that there is no difference between the concentration of SGA near the surface of carpet and in the rest of the home (where other sources also contribute to the concentration). Therefore, children breathing SGA near carpet surfaces does not need to be considered a separate scenario from the general scenario considering indoor inhalation from all sources of SGA. Additionally, the study found that there is no measurable residue of SGA on toys and other objects that children play with on carpet or that come into contact with SGA from household cleaners.

Step 5 – Consideration of Receptors

A major consideration for receptors is the different age groups of children because children's activity patterns, physiology, and dietary habits vary with age. The differing body weights of children affect their exposure because exposure is expressed as mass per body weight per time. Exposure by inhalation is dependent on the ratio of the breathing rate to body weight, which is higher for younger children than older children or adults. Also, children ingest different amounts and different types of food, which affects their ingestion exposure to food. Younger children may engage in activities such as playing on a carpeted floor for long periods of time, which influences their exposure. The breathing zone of children is closer to the floor, and may even be directly next to the floor, depending upon age and type of activity.

Table 5 summarizes body weights, food intake, inhalation rates, and the ratio of the inhalation to body weight for children of different age ranges based on data in EPA's Children's Exposure Factors Handbook (EPA, 2000). These exposure factors are used to generate exposure estimates for different age ranges of children. As the last column of the table shows, the ratio of the inhalation rate to body weight declines as children age, which demonstrates one important reason why age ranges need to be considered in the exposure assessment.

In this case study example, a subpopulation of children who live near the production and manufacturing plants is evaluated for ambient exposures, as this hypothetical example describes higher exposures for this group than other people who are only exposed to the general background levels of SGA. Additionally, the case study example illustrates exposure to breast milk and dermal exposure from playing on carpets that may be principally experienced by infants (or at least infant exposures may be highest versus other age groups).

Step 6 – Consideration of Exposure Durations

The hypothetical toxicity information of SGA indicates that potential hazards of concern include developmental toxicity and neurotoxicity by the oral route, respiratory irritation and carcinogenicity by the inhalation route. For purposes of evaluating exposures in context of potential health hazards, exposure estimates are compared to toxicity criteria (e.g., reference dose, reference concentration). In this case study, SGA is assigned a reference dose of 1 mg/kg/day by the oral route based on neurotoxicity in a long-term (chronic) study. Note that since the reference dose is lower than the level of concern for developmental effects, the reference dose is protective of both neurotoxicity (systemic effects) and developmental effects.

SGA has a very low acute toxicity, and short-term occupational and product related exposures have been shown to not be of concern. Therefore, consideration of only chronic and lifetime-average exposures is sufficient. Because SGA is only carcinogenic via inhalation and not ingestion, lifetime-average exposures were calculated for inhalation only.

Step 7 - Development of Exposure Scenarios

From steps 2 through 6, the array of possible exposure scenarios has been narrowed to the following list. For inhalation exposure, a high-end exposure scenario is considered whereby estimates are made for individuals living near SGA manufacturing plants. In this scenario, both SGA from the manufacturing plant and SGA from indoor usage of SGA-containing products is considered. The chronic exposures refer to exposures averaged over a period of 10 or more years (or the average daily dose), and the lifetime exposure refers to the exposure over a lifetime (lifetime average daily dose). The chronic exposure is for comparison with noncancer benchmarks, and the lifetime exposure is for comparison with cancer benchmarks.

Pathway	Chronic Exposure	Lifetime Exposure	Population of Concern	Significant Subpopulation
Inhalation of ambient air near plants, plus exposure to SGA from indoor sources	X	X	Children	People living near production or manufacturing plants
Ingestion of food*	X		Children	
Ingestion of breast milk*	X		Children	Infants
Dermal contact with carpet*	X		Children	Infants and younger children
Occupational exposure*	X		Pregnant women and offspring	Pregnant women working at production facilities

* Not carcinogenic by ingestion.

The next section presents estimations of the exposure for each of these pathways.

Table 1. Production Volumes, Air Emissions and Water Discharge for the Five SGA Production Facilities for 2000

Plant	Production Volume (tons per year)	Air Emissions (tons per year)	Water Discharge (tons per year)
Whoville	1,000	40	1
Grinch Mountain	200	8	0.2
Horton's Hamlet	350	14	0.35
Lorax Land	400	16	0.4
Suessville	250	10	0.25
Total	2,200	88	2.2

Table 2. Usage Volumes, Air Emissions and Water Discharge for Facilities Using SGA

Usage	Volume (tons per year)	Percent of Total Production	Air Emissions (tons per year)	Water Discharge (tons per year)
Carpet production	300	13.6	2.7	0.2
Household cleaners production	500	22.7	4.5	0.3
Food extraction	400	18.2	3.6	0.2
As a chemical intermediate	1,000	45.5	9.1	0.5
Total	2,200	100	19.9	1.2

Table 3. Summary of Physicochemical Properties of SGA

Property	Value	Reference
Molecular Weight	250 g/mole	Seuss et al. (1987)
Melting Point	NA	Seuss et al. (1987)
Boiling Point	75°C	Seuss et al. (1989)
Vapor Pressure	0.1 mmHg	Seuss et al. (1989)
Partition Coefficient ($logK_{ow}$)	10	Seuss et al. (1989)
Water Solubility	50 ì g/L	Seuss et al. (1988)

Table 4. Summary of Environmental Fate Properties of SGA

Property	Value	Reference
Photodegradation half-life in water	110 days	Seuss et al. (1987)
Hydrolysis half-life in water	110 days at pH 5 90 days at pH 7 45 days at pH 9	Seuss et al. (1987)
Aerobic biodegradation half-life in water	2.5 days	Seuss et al. (1987)
Half-life in atmospheric (reaction with hydroxyl radical)	4 days	Seuss et al. (1987)
Aerobic biodegradation half-life in soil	3 days	Seuss et al. (1987)
Anaerobic biodegradation half-life in soil	30 days	Seuss et al. (1987)

Table 5. Summary of Exposure Factors by Age Group for Children

Age Range	Gender	Body Weight (kg)	Median Food Intake (g/day)	95th Percentile Food Intake (g/day)	Inhalation Rate (m^3/day)	Ratio of Inhalation Rate to Body Weight
Infants	Both	7.1[a]	1100	1800	4.5	0.63
1-2	Both	12.3			6.8	0.55
3-5	Both	17.5	1000	1700	8.3	0.47
6-8	Both	25.2	1100	1900	10	0.40
9-11	Male	35.9			14	0.39
	Female	36.6			13	0.36
12-14	Male	50.4	1100	2300	15	0.30
	Female	50.7			12	0.24
15-18	Male	66.5			17	0.26
	Female	66			12	0.18

[a] In some cases, it may be necessary to use body weights for different age ranges of infants (e.g., 0-6 months, 6-12 months).

C. EXPOSURE ESTIMATION

This section presents detailed exposure assessments and risk characterizations for each of the five scenarios listed in the last section. Key studies used in the exposure assessment are described in Appendices with a standard format. Specifically, each of these appendices includes sections for the following information:

- Title
- Citation
- Study design
- Measurement methodologies
- QA/QC procedures
- Results
- Reliability for exposure assessment

For the purposes of this case study, the level of concern for carcinogenic effects is established at 1 in 100,000 (or 10^{-5}), and the level of concern for noncancer health effects is a hazard index (i.e., the exposure divided by the benchmark toxicological level) of unity. These values were selected for illustrative purposes for this case study and are not meant to signify an explicit level of concern for use in the assessment of a specific chemical in the VCCEP.

The assessment that follows is complete to the level needed to illustrate the concepts in the framework. However, the emphasis is on concepts and not the small details that are required in every exposure assessment.

1. Inhalation of Ambient Air by Residents Living Near Production Facilities

Screening Level Exposure Assessment

Ambient Air

A screening analysis was conducted to estimate the ambient air concentrations in the vicinity of the SGA production facilities. For the purpose of this analysis, the largest production facility, located in Whoville, was chosen to provide an upper-bound of the potential offsite exposure from SGA production and commercial application. The Whoville facility is considered a worst-case for a near facility risk assessment for the following reasons:

- It has the highest air emissions among SGA production facilities (40 tpy, compared to 16 tpy for the next largest emitter).

- The facility is closer to residences in the direction of predominant wind flow than any other SGA production facility.

- It is located in an area with generally low wind speeds and more stable atmospheric conditions, which are both not conducive to air dispersion, than the other SGA production facilities.

To quickly estimate an upper-bound concentration for the Whoville facility, the U.S. EPA's SCREEN3 air dispersion model was used. The SCREEN3 model is frequently used for permitting and other federal and state regulatory applications, and is designed to provide conservative estimates of ambient air concentrations. The SCREEN3 model uses a pre-defined set of meteorological data that reflect the range of dispersion conditions that may be experienced at a site. This obviates the need for site-specific meteorological data.

User specified emission source information is input to the model to estimate the ambient air concentration for each of the pre-defined dispersion conditions. The model estimates the maximum short-term (i.e., 1-hour average) ambient air concentration as a function of distance from the source. For this screening-level analysis, the actual locations of residences or other exposure receptors were not available. Source information, including the stack physical dimensions and effluent rate, were provided by the Whoville facility. The emission estimates were based on process engineering and mass balance calculations using standard EPA methods. Because of the limited routine handling outside of the production area, there are negligible emissions from fugitive sources such as loading/unloading operations and process piping. Therefore, all SGA emissions are from stacks.

The SCREEN3 model does not directly predict long-term ambient air concentrations (i.e, annual average values) because the meteorological input provides no indication of how the dispersion conditions and subsequent air concentrations at a location change over time. When using the SCREEN3 model, longer averaging times more reflective of chronic exposures are calculated using a scaling factor. These scaling factors, which were originally developed for use in permitting under the Clean Air Act, are meant to account for changes in the meteorological conditions (e.g., wind direction and speed) that would occur in nature and result in lower concentrations over time than the maximum predicted for the 1-hour average. For this evaluation, annual average air concentrations were estimated by multiplying the SCREEN3 1-hour averages by a scaling factor of 0.1 as recommended by EPA (EPA, 1992).

The source and receptor information for the Whoville facility is summarized in Table 6. The maximum off-site 1-hour-average predicted by the model was 100 $\mu g/m^3$, which is scaled to a maximum off-site annual-average ambient air concentration of 10 $\mu g/m^3$. Given the conservative assumptions, this estimate is considered to be an upper bound.

Indoor Air

An extensive database of indoor air concentrations of SGA have been collected as part of the U.S. EPA's TEAM study, which included over 500 indoor air measurements made throughout the United States during 1993. The measurements were made in homes in seven different U.S. locations, including Raleigh, North Carolina; Philadelphia, Pennsylvania; St. Louis, Missouri; Minneapolis, Minnesota; Phoenix, Arizona; Los Angeles, California; and Seattle, Washington. Appendix A provides a description of the study methodology and results. For the purposes of risk assessment, the 95^{th} percentile 24-hour average concentration from all sites of 0.02 $\mu g/m^3$ is used. The large majority of homes in the TEAM study were not located near any SGA manufacturing or production facilities; therefore, this concentration predominantly reflects the contribution from indoor sources of SGA such as carpet and household cleaners.

For residences near the SGA manufacturing facilities, it is also necessary to consider the contribution of SGA from ambient air sources infiltrating into indoor air. For a screening level analysis, EPA (1998) recommends a factor of one be used to scale outdoor to indoor concentrations (i.e., the contribution of the outdoor air to the indoor air concentration is simply the outdoor air concentration). In this case, the contribution of the indoor air concentration from indoor sources (0.02 $\mu g/m^3$) is much less than the outdoor air concentration (19 $\mu g/m^3$), so the total estimated exposure is approximately equal to the outdoor air concentration of 10 $\mu g/m^3$.

Screening Level Risk Characterization

The potential human health impacts associated with inhalation exposures in the vicinity of SGA production plants was evaluated using the EPA noncancer reference concentration and cancer unit risk discussed previously. For SGA the inhalation RfC is 1 mg/m^3, which is 100 times higher than the estimated exposure of 10 $\mu g/m^3$ from the Whoville plant. Therefore, there is not a concern for systemic (noncancer) health effects from inhalation exposure for this scenario.

The cancer risk for exposure to the ambient air concentration is calculated as follows:

$$\text{Cancer Risk} = \text{Unit Risk (per } \mu g/m^3) * \text{Concentration } (\mu g/m^3)$$

This is the risk associated with lifetime exposure to the designated concentration.

With a unit risk of $5x10^{-6}$ and an exposure of 10 $\mu g/m^3$, the cancer risk is estimated to be $5x10^{-5}$ (or 1 in 20,000). This risk is greater than the acceptable level of 1 in 100,000; therefore, a refined analysis was conducted to provide a more accurate estimate.

Refined Exposure Assessment

The screening level analysis made a number of simplifying assumptions. In this refined assessment, the following changes were made:

- Instead of using the simple dispersion model SCREEN3, the refined analysis uses the more sophisticated dispersion model ISCST3.

- A survey of the land use around the Whoville facility was conducted to determine the actual locations of residences, schools, and daycare centers where children may potentially be exposed. It was found that the maximum concentration in the screening level analysis was in the boundaries of another industrial facility, where no children would be exposed.

- Because the indoor air contribution from indoor sources is significant for the refined analysis, assumptions about time spent indoors and outdoors for different ages were made.

Ambient Air

A significant source of the conservative bias in the screening level modeling was the application of the SCREEN3 air dispersion model. For the more refined analysis, EPA's ISCST3 air dispersion model was used to predict the annual average air concentrations.

The site-specific meteorological data used in the ISCST3 air model were obtained from the EPA's Support Center for Regional Air Modeling (SCRAM) web site, and reflects the National Weather Service (NWS) observations for the station located nearest to the facility. Following EPA

(1999a) guidance, a period of five years was used in the modeling to ensure that the full distribution of meteorological conditions at the site had been captured, including infrequent worst-case dispersion conditions that yield upper-bound air concentrations for the site.

In the ISCST3 modeling, the emission source, facility fencelines, and areas of residential land use, were modeled using their actual locations, not the nearest distance as was done in the screening analysis with SCREEN3. The ISCST3 model was run for each of the five years of meteorological data and the maximum annual-average ambient air concentration for all potential residential locations at or beyond the facility fenceline was identified. The highest annual-average concentration for residential locations is listed in Table 7 for each year of meteorological data evaluated in the air model. For residential locations, the maximum chronic air concentrations for the five years range from 50 to 100 times lower than the value estimated in the screening level analysis. This reduction in the ambient air concentration is due to the use of actual locations of residential land use and site-specific meteorological data. Recall that in the screening level analysis, the maximum chronic ambient air concentration used for the exposure assessment was predicted to occur within the boundary of another industrial facility, where residential exposures do not occur.

For the purposes of this risk assessment, the chronic residential ambient air concentration used in the inhalation dose estimates was 0.04 ì g/m^3 based on the highest annual-average value for any residential locations around the Whoville facility. This estimate is still considered highly conservative because it is based on the highest annual average and on the location of the highest estimate. Children living in other locations near the facility are expected to have lower exposures.

Indoor Air

As discussed in the screening level analysis, residential indoor air concentrations of SGA are a combination of emissions from indoor consumer use of products containing SGA, and the infiltration of ambient air containing SGA. It was assumed from the TEAM data that an upper bound contribution of SGA from indoor sources is 0.02 µg/m^3. Unlike the screening level analysis, this value is significant compared to the ambient air concentration of 0.04 µg/m^3. Assuming the scaling factor for outdoor infiltration to indoor air, the indoor air concentration is estimated to be 0.06 µg/m^3.

Time-Weighted Daily Air Concentration

The combined dose from the indoor and outdoor air concentrations was estimated using a time-weighted air concentration. The time-weighted air concentration was determined using the ambient and indoor air concentrations and estimates of the fraction of the day an individual spends in each microenvironment. These activity factors as well as the values for inhalation rate and body weight that are used in the inhalation dose equation vary as a function of age, and we need to consider all ages throughout a life to estimate a lifetime average exposure.

Table 8 shows the inputs and results for the calculation of the time-weighted daily air concentration for each age range. Table 9 contains a listing of the remaining exposure factors and the calculated inhalation dose for each age range. Given that SGA is a carcinogen via the inhalation route, the dose estimates for each age range are averaged over a lifetime (i.e., 70 years). The lifetime average daily dose ranged from 5.1×10^{-7} to 9.4×10^{-6} mg/kg/day, depending on age.

Refined Risk Characterization

The screening level analysis showed that there are no concerns for noncancer risk, so only cancer risk is considered in this section.

The unit risk is based on a lifetime exposure of a 70 kg adult with an inhalation rate of 20 m^3/day. Therefore, to evaluate the probability of carcinogenic impacts from SGA inhalation exposures, the unit risk factor for SGA of 5×10^{-6} was converted to a slope factor using the following equation (EPA, 1989):

$$\text{slope factor (mg/kg-day)}^{-1} = \{\text{unit risk per } \mu g/m^3 * \text{BW (kg)}\} / \{\text{inhalation rate } (m^3/\text{day}) * 10^{-3} \text{ mg}/\mu g\}$$

The slope factor equals 0.0175 $(\text{mg/kg-day})^{-1}$, assuming a body weight of 70 kg and an inhalation rate of 20 m^3/day. This value can be compared with the exposure for any age group.

The slope factor was used with the dose calculation for each age range to predict the lifetime excess cancer risk for the exposure period evaluated (i.e., the duration of the age range). Table 10 shows the dose and associated lifetime excess cancer risk for each age range. In addition, assuming the exposure begins at birth, cumulative impacts are shown by summing the risks for each age range. Cumulative impacts are highlighted in Table 10 for 9

years, 30 years and 70 years of exposures. The 9-year and 30-year values reflect the central tendency and high-end estimates, respectively, of residency times in a single dwelling, while the 70 year value reflects the typical number of years assumed for an entire lifetime (EPA, 1999b). The lifetime excess cancer risks for all exposure durations and for the lifetime cumulative exposure were less than the level of concern of $1x10^{-5}$.

Table 6. Overview of the Sources Characteristics of the Whoville Plant

Variable	Selection/Input Value
Source Type Modeled	Point (stack)
SGA Emission Rate	2.2 g/s (40 tons/year)
Stack Height	19.8 m (65 feet)
Stack Diameter	0.9 m (3 feet)
Exit Velocity	6.25 m/s (14 mph)
Exit Temperature	Ambient

Table 7. Maximum Ambient Air Concentration at Residential Land Use Locations from the Refined Modeling of SGA Production Facilities

Year of Meteorological Data	Maximum Annual Average Air Concentrations ($\mu g/m^3$)	Distance from Source to Location of Maximum
1989	0.03	2.0 km Southeast
1990	0.04	2.0 km Southeast
1991	0.02	2.2 km Southeast
1992	0.03	2.0 km Southeast
1993	0.03	2.5 km Northwest

Table 8. Calculation of Average Daily Air Concentration for Residents in the Vicinity of SGA Production Facilities

Age Range (years)	Fraction of Day Spent Outdoors	Ambient Air Concentration (ì g/m³)	Fraction of Day Spent Indoors	Indoor Air Concentration (ì g/m³)	Average Daily Concentration (ì g/m³)[a]
Infants (<1 year)	0.17	0.04	0.83	0.06	0.057
1 to 2	0.17	0.04	0.83	0.06	0.057
3 to 5	0.13	0.04	0.87	0.06	0.057
6 to 8	0.10	0.04	0.90	0.06	0.058
9 to 11	0.08	0.04	0.92	0.06	0.058
12 to 14	0.08	0.04	0.92	0.06	0.058
15 to 18	0.09	0.04	0.91	0.06	0.058
>18 to 30	0.11	0.04	0.89	0.06	0.058
>30 to 70	0.11	0.04	0.89	0.06	0.058

[a] Calculated by summing the product of the fraction of a day spent outdoors and the ambient air concentration with the product of the fraction of a day spent indoors and the indoor air concentration (i.e., for 1 to 2 years = (0.17*0.04 ì g/m³) + (0.83*0.06 ì g/m³) = 0.057 ì g/m³).

Table 9. Inhalation Dose Estimates for Various Age Ranges Based on Refined Air Dispersion Modeling for Residents near SGA Production Facilities

Age Range (years)	Inhalation Rate (m^3/day)	Body Weight (kg)	Exposure Duration (years)	Contribution to Lifetime Average Daily Dose (mg/kg-day) [a]
Infants (<1 year)	4.5	7.1	1	$5.1x10^{-7}$
1 to 2	6.8	12.3	2	$8.9x10^{-7}$
3 to 5	8.3	17.5	3	$1.2x10^{-6}$
6 to 8	10	25.2	3	$9.9x10^{-7}$
9 to 11	13.5	36.25	3	$9.3x10^{-7}$
12 to 14	13.5	50.55	3	$6.7x10^{-7}$
15-18	14.5	63.25	3	$5.7x10^{-7}$
>18 to 30	20	70	12	$2.8x10^{-6}$
>30 to 70	20	70	40	$9.4x10^{-6}$

[a] Calculated as (C_a*IR*ED*365 days/year*10^{-3} mg/µg)/(BW*AT) where C_a = the age-specific average daily air concentration in ì g/m^3; IR = inhalation rate in m^3/day; ED = exposure duration in years; BW = body weight in kg; and AT = averaging time = 25,550 days (i.e., 70 years).

Table 10. Estimates of Lifetime Excess Cancer Risks via Inhalation of SGA for Residents in the Vicinity of SGA Production Plants (Based on Refined Air Modeling)

Age Range (years)	Contribution to Lifetime Average Daily Dose (mg/kg-day)	Excess Lifetime Cancer Risk	
		For Exposure Duration[a]	Cumulative[b]
Infants (<1 year)	5.1×10^{-7}	9.0×10^{-9}	9.0×10^{-9}
1 to 2	8.9×10^{-7}	1.6×10^{-8}	2.5×10^{-8}
3 to 5	1.2×10^{-6}	2.0×10^{-8}	4.5×10^{-8}
6 to 8	9.9×10^{-7}	1.7×10^{-8}	**6.2×10^{-8}**
9 to 11	9.3×10^{-7}	1.6×10^{-8}	7.9×10^{-8}
12 to 14	6.7×10^{-7}	1.2×10^{-8}	9.0×10^{-8}
15-18	5.7×10^{-7}	1.0×10^{-8}	1.0×10^{-7}
>18 to 30	2.8×10^{-6}	5.0×10^{-8}	**1.5×10^{-7}**
>30 to 70	9.4×10^{-6}	1.7×10^{-7}	**3.1×10^{-7}**

[a] Calculated as the product of the SGA slope factor [0.0175 $(mg/kg\text{-}day)^{-1}$] and the lifetime average daily dose for the age range.

[b] Provides an estimate of the increasing risks as exposure duration increases by adding the risk of each successive age range to the sum of the risks for all prior ranges. In this case, it was assumed that the exposure began at birth.

Note: Highlights for cumulative excess lifetime cancer risks at the age ranges of 9 to 11, >18 to 30, and >30 to 70 indicates the approximate risks for the exposure duration corresponding to the central tendency and upper-bound estimates of years of occupancy at a single location (i.e., 9 years and 30 years, respectively) and the default lifetime assumption (i.e, 70 years).

2. Ingestion of Food

SGA is used in commercial food extraction processes and is known to occur in green eggs and ham. The only source of information on the levels of SGA in green eggs and ham is the Total Diet Study (TDS) conducted by the U.S. Food & Drug Administration. TDS is a market basket study that reports the concentrations of compounds in foods purchased at local supermarkets and prepared for consumption as they normally would. Appendix B includes a summary of the methodologies and results of the TDS study for SGA.

Screening Level Exposure Assessment

For the screening level exposure assessment, the 95th percentile residue level for green eggs (100 ppm) and ham (500 ppm) were used.

Average consumption data for both green eggs and ham were obtained from FDA (Samiam, 1992), by different age groups. The values are listed in Table 11. While these data are from a 1990 survey, it is not expected to be significantly different than present values.

Combining the 95th percentile residue concentration and consumption data, the estimated SGA dosage from green eggs and ham consumption for each age group is shown in Table 12. The combined exposure to SGA associated with consumption of green eggs and ham ranged from 0.30 to 1.3 mg/kg/day, depending on the age of the child.

Screening Level Risk Characterization

The exposure and risks for ingestion of SGA in food are shown in Table 12. The highest exposures and risks were for a child in the age range from 3 to 5 years, which resulted in a hazard index greater than one. Exposures to children in the age range from 6 to 11 years also showed a hazard index greater than one. Exposures for all other age ranges resulted in hazard indexes that were less than one. Given that two of the age ranges exceed the risk threshold for this risk assessment (i.e., a hazard index or index of one), and the exposure assessment was based on upper-bound assumptions, a more refined exposure assessment was conducted.

Refined Exposure Assessment

A more refined exposure assessment was conducted for the food ingestion pathway by using stochastic methods. Specifically, a probabilistic assessment

was conducted using the full distribution of values for SGA concentrations in both green eggs and ham, and for consumption rates of these commodities. Distributions for the SGA residue levels in green eggs and ham were developed from the TDS data discussed in the screening level assessment. The shape of the distribution for SGA residue concentrations in both green eggs and ham was determined to be normal. For green eggs, the mean concentration is 15 ppm with a standard deviation of 35 ppm. For ham, the mean concentration is 20 ppm, with a standard deviation of 40 ppm. Table 13 summarizes the mean and standard deviations for the consumption data by age group.

The Monte Carlo sampling program Crystal Ball® was used to generate 10,000 estimates of the SGA dosage from green eggs and ham consumption. In each of the 10,000 runs, a value of the green eggs and ham consumption and residue level was selected from the distributions. It was assumed that the residue levels and the consumption were not correlated. The dosage was calculated as it was in the screening level analysis. The final dosage estimates are shown in Table 14.

Refined Risk Characterization

The hazard indexes for the refined risk characterization are shown in Table 14. For all age ranges, the hazard index was less than one indicating that it is unlikely for exposure to SGA from food ingestion to result in adverse health impacts.

Table 11. Summary of Consumption Data for the Total Diet Study

Commodity	95th Percentile Consumption Rate for Commodity (grams per day)					
	<1 years old	2 year olds	6 year olds	10 year olds	14 to 16 year olds	
					Male	Female
Green eggs	20	30	120	160	190	165
Ham	0.27	4	20	30	30	28
Sum of Consumption	20.27	34	140	190	220	193

Table 12. Screening Level Estimation of Ingestion Exposure Associated with SGA in Food

Age (years)	Body Weight (kg)	Green Eggs			Ham			Total SGA Exposure from Food (mg/kg/day)	Hazard Index
		Concentration of SGA (mg/kg)	Consumption (g/day)	SGA Exposure (mg/kg/day)	Concentration of SGA (mg/kg)	Consumption (g/day)	SGA Exposure (mg/kg/day)		
<1	7.1	100	20	0.28	500	0.27	0.02	0.30	0.30
1-2	12.3	100	30	0.24	500	4	0.16	0.41	0.41
3-5	17.5	100	120	0.69	500	20	0.57	1.26	1.3
6-11	30.7	100	160	0.52	500	30	0.49	1.01	1.0
12-19	57.0	100	190	0.33	500	30	0.26	0.60	0.60

Table 13. Descriptive Statistics for Consumption of Food Used to Estimate the SGA Ingestion Exposures in the Refined Assessment

Age (years)	Green Eggs Consumption Rate (g/day)		Ham Consumption Rate (g/day)	
	Mean	Standard Deviation	Mean	Standard Deviation
<1	8	5	0.01	3
1-2	12	18	1	23
3-5	45	12	3	15
6-11	60	18	8	6
12-19	65	20	8	4

Table 14. Summary of Refined Exposure Assessment Estimates for SGA Ingestion Exposure from Green Eggs and Ham Consumption

Age (years)	SGA Food Exposure (mg/kg/day)		Hazard Index
	Mean	95th Percentile	
<1	0.017	0.051	0.051
1-2	0.016	0.052	0.052
3-5	0.042	0.133	0.13
6-11	0.035	0.114	0.11
12-19	0.020	0.065	0.065

3. Ingestion of Breast Milk by Infants

Screening Level Exposure Assessment

Whoville Industries monitored its employees that work in its manufacturing plant in Whoville for exposure, including measurements of SGA in blood (Whoford and DeWho, 1999). Due to SGA's presence in blood, there is a concern that SGA may be in breast milk consumed by infants. Therefore, the blood measurements made by Whoville Industries were used to estimate exposure of infants to breast milk. The Whoville Industries plant is similar to the other SGA production facilities in regard to chemical processes, and health and safety procedures. Therefore, data form the Whoville plant is considered representative of the other SGA plants.

Appendix C provides a summary of the Whoville Industries study. Because this study monitors workers at the largest manufacturing facility, it is considered to provide upper-bound exposure estimates. For a screening-level exposure assessment, the upper 95th percentile value of the female blood concentration of 0.1 µg/L is used. Also, Whoferling (1994) measured a milk/blood partition coefficient of 1.5; therefore, the breast milk concentration is estimated to be 0.15 µg/L (0.1 µg/L * 1.5). The dose to children is estimated as follows:

Dose (mg/kg/day) = {Milk Concentration (µg/L) * Breast Milk Consumption (L/day) * 0.001 mg/µg }/ {Body Weight (kg)}

In EPA's draft Children's Exposure Factors Handbook (EPA, 2000), the upper percentile estimate of breast milk consumption is 980 mL/day (or 0.98 L/day), as an average over the first year of life for a child who consumes breast milk. Given the 95th percentile milk concentration of 0.15 µg/L and a body weight of 7.1 kg for an infant, the estimated dose of SGA from breast milk consumption is $2x10^{-5}$ mg/kg/day.

Screening Level Risk Characterization

The exposure estimate of $2x10^{-5}$ mg/kg/day is substantially below the reference dose of 1 mg/kg/day (by nearly 50,000 fold). Given that this calculation is very conservative (based on upper percentile exposure from largest manufacturing plant and upper percentile breast milk consumption), exposure to breast milk is not considered to be a concern.

4. Dermal Contact with Carpet

SGA is used in the manufacturing of carpets and a small residue of the SGA remains after installation of the carpet. Children playing on carpets may come in dermal contact with the SGA residue and be exposed. Dermal exposure to children playing on the carpet can be estimated with knowledge of the dislodgeable residue (*DR*) concentration, dermal transfer factor (T_c), activity factor (i.e., hours per day of dermal contact), dermal absorption coefficient (DAC), and body weight (BW), as follows (EPA, 1999c):

Dermal Dose (mg/kg/day) = *DR* (μg/cm^2) * T_c (cm^2/hr) * Activity Factor (hr/day) * 0.001 mg/μg * DAC/ BW (kg) (1)

EPA recommends a default transfer factor for children playing on carpet of 5,000 cm^2/hr (EPA, 1999). The dermal absorption coefficient of SGA has not been measured; therefore a default value of 100 percent is assumed.

Loraxium Carpet Manufacturers (LCM), the largest manufacturer of carpets with SGA in the United States, sponsored a study to estimate the *DR* on fresh carpet for SGA (XYZ Laboratories, 1997). A complete description of this study is provided in Appendix D. In this study, *DRs* were measured on 25 freshly installed carpets. The median *DR* was 0.4 μg/cm^2, and the 95th percentile *DR* was 1.0 μg/cm^2. To provide a conservative assessment, the upper 95th percentile *DR* concentration (1 μg/cm^2) is used for the risk assessment.

The Carpet Manufacturers Dermal Exposure Task Force (CMDETF) has developed estimates of the amount of time children spend playing on carpeted surfaces based on a survey of 200 parents (CMDETF, 1996). A complete description of the study is found in Appendix E. Because an upper-percentile value was already used for the *DR* concentrations, median values were used for the amount of time children spend playing on carpeted surfaces. The median values were as follows by age groups: (1) infants: 5.0 hours, (2) 1-2: 4.0 hours, (3) 3-5: 3.0 hours, (4) 6-8: 2.0 hours, (5) 9-11: 1.0 hour, (6) 12-14: 1.0 hour, and (7) 15-18: 1.0 hour.

The results from the LCM report, all of the other accompanying exposure factors and the exposure estimates using equation 1 are shown in Table 15. The calculations were also performed using upper-percentile values for the activity factor and median values of the DR concentration (not shown), and the results were lower.

Screening Level Risk Characterization

Table 15 presents the hazard indices for all age groups in the last column. The results show that the hazard indices for infants and 1-2 year olds are above unity, indicating a possible concern. The hazard indices for the older children were all below the level of concern. Given the high-end values used for *DRs*, and the default assumption of 100 percent absorption, the assessment is considered highly conservative. A refined assessment was conducted to further evaluate the potential concerns for infants and 1-2 year olds.

Refined Exposure Assessment

The default dermal absorption coefficient of 100 percent that was used in the screening-level risk assessment is considered to be a highly conservative value used in lieu of actual measurements. Therefore, LCM conducted an *in vivo* dermal absorption study (XYZ Laboratories, 2001) to refine the screening-level assessment (see Appendix F for details). The study was conducted in five human volunteers, and the average dermal absorption coefficient was 3 percent, with very little variability between measurements. The refined exposure estimates are shown in Table 16.

Refined Risk Characterization

The risk estimates are shown in Table 16. The refined hazard indices are below unity for all age groups. Therefore, the use of the new *in vivo* results has shown that the exposures are below the level of concern.

Table 15. Summary of Screening-Level Exposure Estimates for Children Playing on Carpeted Surfaces

Age	DR (mg/cm^2)[a]	T_c (cm^2/hr)[b]	Dermal Absorption Coefficient[c]	Activity Factor (hr/day)[d]	Body Weight (kg)	Dose (mg/kg/day)	Hazard Index[e]
Infants	1.0	5,000	1.0	5	7.1	3.52	3.5
1-2	1.0	5,000	1.0	4	12.3	1.63	1.6
3-5	1.0	5,000	1.0	3	17.5	0.86	0.86
6-8	1.0	5,000	1.0	2	25.2	0.40	0.40
9-11	1.0	5,000	1.0	1	36.3	0.14	0.14
12-14	1.0	5,000	1.0	1	50.55	0.099	0.10
15-18	1.0	5,000	1.0	1	66.25	0.075	0.08

[a] XYZ Laboratories, 1997 (upper 95th percentile measurement)

[b] EPA, 1999 (default value)

[c] Default value

[d] CMDETD, 1996 (average value)

[e] Hazard index is the exposure over the reference dose of 1 mg/kg/day

Table 16. Summary of Refined Exposure Estimates for Children Playing on Carpeted Surfaces

Age	DR (mg/cm^2 of carpet surface)[a]	T_c (cm^2/hr)[b]	Dermal Absorption Coefficient[c]	Activity Factor (hr/day)[d]	Body Weight (kg)	Dose (mg/kg/day)	Hazard Index[e]
Infants	1.0	5,000	0.03	5	7.1	0.11	0.11
1-2	1.0	5,000	0.03	4	12.3	0.049	0.049
3-5	1.0	5,000	0.03	3	17.5	0.026	0.026
6-8	1.0	5,000	0.03	2	25.2	0.012	0.012
9-11	1.0	5,000	0.03	1	36.3	0.0041	0.0041
12-14	1.0	5,000	0.03	1	50.55	0.0030	0.0030
15-18	1.0	5,000	0.03	1	66.25	0.0023	0.0023

[a] XYZ Laboratories, 1997 (upper 95th percentile measurement)

[b] EPA, 1999 (default value)

[c] XYZ Laboratories, 2001

[d] CMDETD, 1996 (average value)

[e] Hazard index is the exposure over the reference dose of 1 mg/kg/day

5. Occupational Exposure to Pregnant Women

Screening Level Exposure Assessment

SGA is a developmental toxicant. In a rat study, there were malformations in the offspring after exposure to the dams. Therefore, it is necessary to assess exposure to pregnant women to evaluate whether there could be effects in offspring. The Whoville Industries study (previously described in Appendix C) provides exposure estimates for women from urine metabolite estimates. Specifically, for 28 occupationally exposed women at the largest SGA manufacturing plant, the average exposure was 0.5 mg/kg/day, and the upper 95^{th} percentile exposure was 1.3 mg/kg/day. Because the Whoville plant is the largest SGA manufacturing facility and has typical industrial hygiene practices within the industry, and because the women that work at the plant likely are exposed to relatively high ambient concentrations of SGA, the upper 95^{th} percentile is considered to be a conservative estimate of the exposure for pregnant women.

Screening Level Risk Characterization

The level of concern for developmental toxicity is 5 mg/kg/day. For an upper bound exposure of 1.3 mg/kg/day, the hazard index is 0.26. This value is below unity and thus within the margin of safety.

D. AGGREGATE ASSESSMENT

Exposure Assessment

Because there are multiple exposure pathways that could lead to a combined aggregate exposure for SGA, an aggregate exposure assessment was considered and conducted. The aggregate assessment considers exposure from four pathways for children: (1) inhalation (assumed to be 100 percent absorbed), (2) ingestion of food with SGA residues, (3) ingestion of breast milk, and (4) dermal contact with carpet (assuming 3 percent dermal absorption, as per the *in vivo* study). The results are shown in Table 17 for each age range. The exposures range from 0.067 (15 to 18 year olds) to 0.16 (infants). Upper percentile estimates for each pathway were used, which makes this a very conservative aggregate assessment. For younger children, dermal contact with carpet is the largest contributor to the aggregate exposure. For older children, food ingestion is the largest contributor.

Risk Characterization

The hazard indexes are shown in Table 17 in the last column. All hazard indexes are below unity; therefore, aggregate exposures to SGA are not of concern.

Table 17. Summary of Aggregate Exposure Assessment and Risk Characterization

Age	Exposure (mg/kg/day)					Aggregate Hazard Index
	Inhalation	Food Ingestion	Breast Milk	Carpet	Aggregate Exposure	
Infants	$3.8x10^{-5}$	0.051	$2.0x10^{-5}$	0.11	0.16	0.16
1-2	$3.3x10^{-5}$	0.052	0.0	0.049	0.10	0.10
3-5	$2.8x10^{-5}$	0.13	0.0	0.026	0.16	0.16
6-8	$2.4x10^{-5}$	0.11	0.0	0.012	0.13	0.13
9-11	$2.2x10^{-5}$	0.11	0.0	0.0041	0.12	0.12
12-14	$1.6x10^{-5}$	0.065	0.0	0.0030	0.068	0.068
15-18	$1.4x10^{-5}$	0.065	0.0	0.0023	0.067	0.067

E. UNCERTAINTY ASSESSMENT

The goal of the exposure assessment was to estimate upper-bound exposures for children of various age groups, and for pregnant women. However, when there were uncertainties, conservative assumptions were made. Table 18 summarizes the key uncertainties in the exposure assessment. For the ingestion of green eggs and ham scenario, data were available to make a reasonably accurate estimate of the 95th percentile concentration. For the other exposure scenarios for children, the exposure estimates combine several high-end estimates for input parameters, which likely makes the estimates greater than the 95th percentile. For occupational exposure to pregnant women, the exposure is a reasonable estimate of the 95th percentile for women working at the largest SGA production plant.

Table 18. Summary of Uncertainties in the Risk Assessment

Exposure Pathway	Key Uncertainties	Overall Assessment of Uncertainty
Inhalation of ambient air near SGA production facilities and indoor air from SGA indoor products	• ISC dispersion model is accurate to about a factor of two • Emission rates are based on EPA estimation methods with unknown uncertainties • SGA usage in household cleaners has been reduced since the TEAM study, thus the indoor concentrations measured in that study may be high for current usage	The estimates are based on conservative assumptions. In particular, the exposure estimate is based on the highest 5-year value and on the location near the SGA plant with the highest concentration. Children living in other locations near the plant likely have lower exposures. Combined with a 95th percentile indoor air concentration, this exposure is conservative.
Ingestion of food	• Use of half of the limit of detection for residue samples in the TDS study that were non-detects. • Use of 1991 consumption data, which may not reflect current consumption • Assumption that residue concentrations and consumption are not correlated, without data to validate	The estimates of food ingestion are likely to be quite accurate. The use of the full distribution of residue and consumption data should result in a fairly accurate picture of the exposure distribution.

Exposure Pathway	Key Uncertainties	Overall Assessment of Uncertainty
Ingestion of breast milk	• Milk/blood partition coefficient was based on only one measurement. • Blood measurements from only one production plant (though the largest)	The use of a 95th percentile blood concentration from women in the largest SGA production plant, combined with the upper percentile breast milk concentrations makes this a conservative estimate.
Dermal contact with carpet	• Use of default transfer factor • No knowledge of specific activities that children in the activity factor study engaged in	Given that the 95th percentile values were used for the dislodgeable residue and the activity factor, this is likely a conservative estimate. However, the use of the default transfer factors adds uncertainty. A biomonitoring study would have been ideal, but these are difficult to conduct and base risk assessments on.
Occupational exposure for pregnant women	• Exposure measurements from only one production plant (though the largest)	Use of 95th percentile, chemical-specific exposure data make this an accurate and conservative assessment.

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Please note that these references are mostly hypothetical and fictitious.

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Appendix A. Summary of the Total Exposure Assessment Monitoring (TEAM) Study

Title	Total Exposure Assessment Monitoring (fictitious description based on actual study)
Citation	Report published by the Environmental Protection Agency, 1995
Study Objective	To measure the concentrations of air pollutants in residential indoor air environments
Study Design	In seven U.S. cities, investigators measured residential indoor air concentrations throughout 1993 (all seasons) in 75 homes in each city. The cities include Raleigh, North Carolina; Philadelphia, Pennsylvania; St. Louis, Missouri; Minneapolis, Minnesota; Phoenix, Arizona; Los Angeles, California, and Seattle, Washington. In each home, samples were taken in the kitchen, living room, bathroom, and bedroom. All samples were 24-hour averages.
Measurement Methodologies	SGA was measured by SW 846, Method 9988, and analyses were performed by Lorax Laboratories. The detection limit was 0.001 ì g/m^3, and the recovery of spiked samples was over 90 percent.
QA/QC Procedures	Field blanks and duplicates samples were taken. Field fortifications were made to determine storage stability and recovery. Recovery for SGA was 90 percent.
Results	Within a given home, the TEAM measurements did not vary significantly from room to room. Therefore, the concentrations were averaged for the different rooms in the house. The 95th percentile and maximum concentrations are shown below for each city, and overall: City — 95th Percentile (ì g/m^3) — Maximum (ì g/m^3) Raleigh, NC — 0.020 — 0.040 Philadelphia, PA — 0.030 — 0.036 St. Louis, MO — 0.020 — 0.031 Minneapolis, MN — 0.010 — 0.023 Phoenix, AZ — 0.020 — 0.029 Los Angeles, CA — 0.020 — 0.036 Seattle, WA — 0.020 — 0.040 Overall — 0.020 — 0.040

Reliability for Exposure Assessment	The measurements were sufficiently accurate and precise. There are 525 measurements in seven different U.S. cities. Therefore, the data are adequate to be representative of the U.S.

Appendix B. Summary of the "FDA's Total Diet Study"

Title	FDA's Total Diet Study
Citation	FDA Report Publication No. 876-2001, 2001
Study Objective	To quantify the residue concentration of a variety of chemicals on food commodities that people consume.
Study Design	The study has been ongoing since 1991. In each year, at least three cities are selected for analysis. Researchers go to local supermarkets and purchase a pre-determined list of food commodities. Some commodities are analyzed raw, and some meals are prepared using standard recipes. The meal preparation is followed by chemical analysis.
Measurement Methodologies	SGA was measured by SW 846, Method 9988, and analyses were performed by Lorax Laboratories. The detection limit was 0.001 ì g/m^3, and the recovery of spiked samples was over 90 percent.
QA/QC Procedures	Field blanks and duplicates samples were taken. Field fortifications were made to determine storage stability and recovery. Recovery for SGA was 90 percent.
Results	The TDS measurements for SGA were made for 83 commodities, including prepared meals. SGA was found in only 2 of the 83 commodities, specifically green eggs and ham. In green eggs, SGA was detected in 977 of 1,551 samples (63 percent) and it was found in 1,242 of 1,725 samples (72 percent) of ham (since 1991, the start of the study). Summary statistics for the green eggs and ham sampling results are listed below. For non-detects, half the limit of detection (LOD) was used (LOD = 0.01 ppm) in calculating summary statistics.

Commodity	Detection Rate	Mean (ppm)	95th Percentile (ppm)
Green eggs	977 of 1,551	15	100
Ham	1,242 of 1,725	20	500

Reliability for Exposure Assessment	The measurements were sufficiently accurate and precise. There are 1,551 measurements in green eggs and 1,725 measurements in ham. These data were collected in a variety of U.S. cities over the last 10 years. Therefore, the mean and 95th percentile should be representative of the U.S.

Appendix C. Summary of the Occupational Exposure Study to SGA at the Manufacturing Plant in Whoville

Title	Occupational Exposure to SGA at a Manufacturing Plant in Whoville
Citation	*Occupational Health Perspectives*, **25**, 223-256, 1999
Study Objective	To measure the SGA exposure to workers at the Whoville manufacturing plant.
Study Design	For 93 workers, measurements of SGA in blood were made before and after three separate, normal workdays. Of the 93 workers, 28 were female. Additionally, measurements of the urinary metabolite SGA-CA were made for all of these individuals before and after the workday.
Measurement Methodologies	Blood samples were drawn by needle and urine samples were collected following the workday. SGA was measured in blood by SW 846, Method 9999, and analyses were performed by Lorax Laboratories. SGA-CA was measured in urine by SW 846, Method 9999.
QA/QC Procedures	QA/QC procedures included blind duplicates for every 10^{th} sample. Also, storage stability was evaluated by fortifying samples that were stored and shipped along with the field samples. This was all done for both blood and urine samples.
Results	For all workers, the average blood level concentration was 0.04 ppb (or µg/L) with the upper 95^{th} percentile concentration of 0.8 µg/L. The results for women only were 0.05 µg/L for the median, and 0.1 µg/L for the 95^{th} percentile. The pre-work measurements showed lower levels, particularly following days off, indicating that SGA does not build up in the blood stream. From the urinary metabolite data, the exposure to SGA was calculated based on the known metabolism of SGA (75 percent is secreted as SGA-CA) (see Whoton and Whodidit, 1995). For all workers, the average exposure was 0.3 mg/kg/day, and the upper 95^{th} percentile was 0.9 mg/kg/day. For women only, the average exposure was 0.5 mg/kg/day, and the upper 95^{th} percentile was 1.3 mg/kg/day.

Reliability for Exposure Assessment	The measurements were sufficiently accurate and precise. The measurements were made at the largest SGA production facility in the U.S. The industrial hygiene practices, ventilation rates, and building sizes are similar at the Whoville facility compared to other SGA production facilities in the U.S. Therefore, these data are considered representative of exposure to SGA of anyone working at an SGA production facility.

Appendix D. Summary of "Measurement of Potential Exposure Parameters Associated with SGA in Carpet, "

Title	Measurement of the Potential Exposure Parameters Associated with SGA in Carpet
Citation	XYZ Laboratories Study Report 12345-97, 1997
Study Objective	To make the following measurements associated with SGA in carpet: 1) dislodgeable residue (*DR*) of SGA on freshly installed carpet surfaces to allow an estimation of the dermal exposure of children playing on the carpets. 2) air concentration of SGA in area directly above fresh carpet that a child may breath while playing on carpet 3) concentration of SGA on toys and other objects that children may mouth and that could have residues from SGA in carpet or from household cleaners
Study Design	Volunteers were solicited by newspaper ads in the Boston area. For each volunteer, arrangements were made to visit the home within a week of new carpet being installed. At each of the 25 homes, researchers collected five samples of *DRs* using a roller. The roller is rolled across the carpet and collects the *DRs* on the surface of the roller. The researchers also collected three SGA air concentration measurements about an inch from the carpet and three air concentration measurements in the normal adult breathing zone about the carpet (about 5 to 6 feet). Additionally, the researchers made measurements of SGA residues on several toys and other objects used by children in each home.
Measurement Methodologies	SGA was extracted from the roller surfaces and toys and other objects used by children using acetonitrile. SGA was subsequently measured in the acetonitrile solution using Analytical Method SW 846, 9999. The detection limit was 0.01 µg/L, and all measurements were above the detection limit. In air, SGA was measured by SW 846, Method 9988, and analyses were performed by Lorax Laboratories. The detection limit was 0.001 ì g/m^3, and the recovery of spiked samples was over 90 percent.

QA/QC Procedures	QA/QC procedures included blind duplicates for every 10th sample. Also, storage stability was evaluated by fortifying samples that were stored and shipped along with the field samples. Recovery for SGA was 95 percent for both air and residue samples.
Results	The *DR* results are as follows: Mean: 0.3 μg/cm^2 Median: 0.4 μg/cm^2 95th Percentile: 1.0 μg/cm^2 The average indoor air concentration near the surface of the carpet was 0.053 μg/m^3, and the average in the normal adult breathing zone was 0.054 μg/m^3. Therefore, it was concluded that the concentration of SGA near the carpet was not higher than the normal air in the homes. While the contribution from the carpet may be higher closer to the carpet, it is likely that SGA from other sources results in the similar concentration for the rest of the home. All of the measurements of SGA residues on toys and other objects were non-detectable.
Reliability for Exposure Assessment	The measurements were sufficiently accurate and precise. Measurements were made in 25 homes with different carpet types that use SGA. Although all measurements were made in the Boston area, there is not expected to be a geographical difference in these measurements. Therefore, the results are considered representative of the U.S.

Appendix E. Summary of "A Survey of the Amount of Time Children Spend Playing on Carpet Surfaces"

Title	A Survey of the Amount of Time Children Spend Playing on Carpet Surfaces
Citation	Carpet Manufacturers Dermal Exposure Task Force Study No. 111-96, 1996
Study Objective	To provide estimates of the amount of time children spend playing on carpet surfaces. These estimates are used in risk assessments of dermal exposures for children to chemicals in carpets.
Study Design	A advertisement was placed in *Family Circle* magazine (a national publication) to recruit 200 parents to collect diary data on the amount of time children spend playing on carpeted surfaces. The parents collected diaries over three, non-consecutive days, and mailed the information back to the study researchers for analysis.
Measurement Methodologies	Not applicable.
QA/QC Procedures	For a subset of the children (20), investigators followed up with the parents after receiving the diaries and asked questions to ensure that the information in the diaries was correctly and accurately obtained.
Results	The amount of time children spend playing on carpeted surfaces was as follows: All values are in hours. Age / Mean / Median / 95th Percentile Infants: 5.2 / 5.0 / 8.0 1-2: 3.9 / 4.0 / 7.1 3-5: 3.4 / 3.0 / 4.4 6-8: 2.1 / 2.0 / 3.4 9-11: 0.8 / 1.0 / 1.7 12-14: 1.0 / 1.0 / 1.9 15-18: 1.1 / 1.0 / 2.1
Reliability for Exposure Assessment	The follow-up interviews with the 20 parents demonstrated the reliability of the survey instrument for collecting the data. With over 200 children represented in the study, the results are considered representative of the U.S.

Appendix F. Summary of "*In Vivo* Dermal Absorption of SGA"

<table>
<tr><td>Title</td><td>In Vivo Dermal Absorption of SGA</td></tr>
<tr><td>Citation</td><td>XYZ Laboratories Report No. 456-2001, 2001</td></tr>
<tr><td>Study Objective</td><td>To estimate the percentage absorption of a dermally applied dosage of SGA</td></tr>
<tr><td>Study Design</td><td>Five human volunteers were recruited. SGA was topically administered on a 2 cm^2-shaved patch of skin, nominally at 15 mg/cm^2. Urine samples were subsequently collected, and the concentration of SGA-carboxylic acid (SGA-CA), the principal metabolite of SGA, were collected.</td></tr>
<tr><td>Measurement Methodologies</td><td>SGA-CA in urine was analyzed with Method SW 846, 9999, and the detection limit was 0.01 µg/L. All samples were above the detection limit.</td></tr>
<tr><td>QA/QC Procedures</td><td>Field blanks and duplicates samples were taken. Field fortifications were made to determine storage stability and recovery. Recovery for SGA was 90 percent.</td></tr>
<tr><td>Results</td><td>The amount of SGA-CA in urine can be used to estimate the SGA exposure. The conversion of SGA to SGA-CA occurs with 1:1 stoichiometry (Whoton and Whodidit, 1995), and the ratio of the molecular weight of SGA to SGA-CA is 0.88.

The results of the measurements are as follows:

<table>
<tr><th>Amount Applied Per cm^2 (mg/cm^2)</th><th>Total Amount Applied (mg)[a]</th><th>SGA-CA Excreted (mg)</th><th>SGA-Equivalent Excreted (mg)[b]</th><th>Dermal Absorption Coefficient (percent)</th></tr>
<tr><td>5.0</td><td>20.0</td><td>0.90</td><td>0.60</td><td>3.0</td></tr>
<tr><td>5.1</td><td>20.4</td><td>0.84</td><td>0.55</td><td>2.7</td></tr>
<tr><td>4.8</td><td>19.2</td><td>0.96</td><td>0.63</td><td>3.3</td></tr>
<tr><td>5.2</td><td>20.8</td><td>0.92</td><td>0.61</td><td>2.9</td></tr>
<tr><td>4.9</td><td>19.6</td><td>0.92</td><td>0.61</td><td>3.1</td></tr>
<tr><td></td><td></td><td></td><td>Average</td><td>3.0</td></tr>
</table>
[a] Based on a 4 cm^2 topically applied area
[b] Based on a molecular weight ratio of 0.88 (SGA/SGA-CA) and a 75 percent conversion of SGA to SGA-CA (see Whoton and Whodidit, 1995).</td></tr>
</table>

Reliability for Exposure Assessment	The measurements made in the study were sufficiently accurate and precise. The study was conducted according to Good Laboratory Practices (GLP). Given the very small variability in dermal absorption among the subjects, the sample size of five is considered sufficient to be representative of the U.S. population.